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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,806	04/18/2001	Sudhir Agrawal	HYZ-069CN (47508-407)	8489

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/837,806	AGRAWAL, SUDHIR	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-11,14-16,18-26 and 29-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-11,14-16,18-26 and 29-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office action is in response to the communications filed 9-24-03.

Claims 1, 4-11, 14-16, 18-26, 29-39 are pending in the instant application.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-24-03 has been entered.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections and Rejections Necessitated by Amendments

Applicant's arguments, filed 9-24-03, with respect to the rejection(s)of claim(s) 1-15, 31-36 under 112, first and second paragraphs, and 103 have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, new ground(s) of rejection are made in view of written description,

indefiniteness and lack of enablement regarding the ability to inhibit HIV-2 in vitro or in vivo using the antisense oligonucleotides instantly claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-11, 14-16, 17-26, 29-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 2 and in claim 16, line 5, it is unclear what the term "specifically complementary" means, therefore the metes and bounds of the claimed subject matter cannot be determined (e.g. perhaps replacing "specifically complementary to" with --completely complementary to a consecutive 21 nucleobase portion of --would be remedial).

In claims 8-11 and 23-26, line 1, it is unclear what the term "having" or "has" is referring to (e.g. perhaps replacing "having" or "has" with –consisting of—would be remedial).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-11, 14-16, 17-26, 29-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to compositions and methods comprising 21 nucleobase oligonucleotide sequences *specifically complementary to* the nucleotide of SEQ ID NO: 5.

The specification and claims do not describe the elements that are essential to the genus comprising oligonucleotides specifically complementary to the nucleotide of SEQ ID NO: 5, nor do they describe the distinguishing attributes concisely shared by the members of this broad genus. The scope of the claims includes numerous structural variants, and genus is highly variant because a significant number of structural differences between members of the genus is permitted. Concise structural features that could distinguish structures or compounds within the genus from others are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is need. The specification and claims fail to adequately describe a representative number of species in the genus comprising nucleobase oligonucleotide sequences specifically complementary to the nucleotide of SEQ ID NO: 5, and because the genus is highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of

species to describe the genus claimed. Thus, applicant was not in possession of the claimed genus.

Claims 14, 15, 34-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions and methods of inhibiting HIV-1 infection in a cell in vitro or in vivo comprising directly contacting the cell with a 21 nucleobase oligonucleotide completely complementary to a consecutive 21 nucleobase portion of SEQ ID NO: 5, and which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides, does not reasonably provide enablement for compositions and methods of inhibiting HIV-2 infection in a cell comprising contacting the cell with a 21 nucleobase oligonucleotide specifically complementary to SEQ ID NO: 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to compositions and methods of inhibiting HIV-1 or HIV-2 infection in a cell comprising contacting the cell with a 21 nucleobase oligonucleotide specifically complementary to a consecutive 21 nucleobase portion of SEQ ID NO: 5, and which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The state of the prior art and the predictability or unpredictability of the art. In addressing the obviousness rejection made by the Examiner in the prior Office action mailed 8-28-02, Applicants have argued in their communication filed 9-24-03 (on page 15) that Hovanessian et al (USPN 5,470,702) teaches away from the expectation that the in vitro inhibition of gag expression by antisense that specifically targets HIV-1 gag would lead to the in vitro inhibition of HIV-1 and HIV-2 replication in vitro, because of the differences in the nucleotide sequences between the two viruses (40% homology). In addition, the specification teaches the inhibition of HIV-1 infection in vitro following the administration of a 21 nucleobase oligonucleotide completely complementary to a consecutive 21 nucleobase portion of SEQ ID NO: 5, and which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides. Therefore, the instantly claimed invention is rejected for lacking enablement over the scope claimed.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of inhibiting HIV-2 infection in vitro or in vivo comprising contacting a cell with a 21 nucleobase oligonucleotide specifically complementary to SEQ ID NO: 5, which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides.

The specification teaches the inhibition of HIV-1 infection in vitro comprising the administration of antisense oligonucleotides a 21 nucleobase oligonucleotide completely

complementary to a consecutive 21 nucleobase portion of SEQ ID NO: 5, and which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides. The specification also teaches protocols for testing the stability of these antisense oligonucleotides in an organism following oral administration of radioactively labeled oligonucleotides. The specification fails to teach the inhibition of infection of HIV-2 in vitro or in vivo comprising the administration of the instantly claimed antisense oligonucleotides. One skilled in the art would not accept on its face the examples given in the specification of the in vitro inhibition of expression of nucleic acids encoding gag of HIV-1 or the in vitro inhibition of HIV-1 infection following administration of a 21 nucleobase oligonucleotide completely complementary to SEQ ID NO: 5, which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides, to cells in culture as being correlative or representative of the successful inhibition of infection of HIV-2 in view of the lack of guidance in the specification and known unpredictability associated with the ability to predict the successful inhibition of HIV-2 infection comprising the administration of the instantly claimed antisense oligonucleotides. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with in inhibition of HIV-2 provided by antisense administered, and specifically regarding the instant compositions and methods claimed.

The breadth of the claims and the quantity of experimentation required.

The breadth of the claims is very broad. The claims are drawn to methods of inhibiting

HIV-1 and HIV-2 infection in a cell comprising contacting the cell with an antisense oligonucleotide consisting of 21 nucleotides which is specifically complementary to nucleotides 324-345 of gag of the HIV-1 genome set forth as SEQ ID NO: 5, which nucleotides within the oligonucleotide are linked via phosphorothioate internucleotide linkages, and at least two 2'-substituted 5'-terminal ribonucleotides. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of the ability to target and inhibit HIV-2 infection in cells comprising direct administration of the instantly claimed antisense whereby HIV-2 inhibition is provided. Since the specification fails to provide any particular guidance for the successful inhibition of HIV-2 infection in a cell, it would require undue experimentation to practice the invention over the scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

JZ

12/15/03